

AMENDMENTS TO THE SPECIFICATION:

Please replace the title:

Cystine Knot Growth Factor Mutants

with the following new title:

Isolated Modified Human Chorionic Gonadotropin Proteins

Please amend the paragraph beginning at page 5, line 7 (carrying over to page 6, line 4) as follows:

Compositions and methods based on mutant Cystine Knot Growth Factors (CKGFs) comprising amino acid substitutions relative to the wild type hormone/growth factor. Mutated glycoprotein hormones, including thyroid stimulating hormone (TSH) and chorionic gonadotropin (CG) are disclosed as exemplary mutant CKGFs. Mutant TSH heterodimers and [[hCH]] **hCG** heterodimers possessed modified bioactivities, including superagonist activity. Additionally, a variety of mutant CKGF family proteins are disclosed. For example, mutant CKGF proteins disclosed include mutant platelet-derived growth factor (PDGF) family proteins such as mutant PDGF homo- and heterodimers, and mutant vascular epithelial cell growth factor (VEGF) proteins; mutant neurotrophin family proteins such as mutant nerve growth factor (NGF), mutant brain-derived neurotrophic factor (BDNF) proteins, and mutant neurotrophin-3 (NT-3) and mutant neurotrophin-4 (NT-4) proteins; mutant transforming growth factor- β (TGF- β) family proteins such as mutant TGF- β 1, mutant TGF- β 2, mutant TGF- β 3, mutant TGF- β 4/ebaf, mutant neurturin, mutant inhibin A, mutant inhibin B, mutant Activin A, mutant Activin B, mutant Activin AB, mutant Mullerian inhibitory substance (MIS), mutant bone morphogenic Protein-2 (BMP-2), mutant bone morphogenic protein-3 (BMP-3)/osteogenin, mutant bone morphogenic protein-3b (BMP-3b), mutant bone morphogenic protein-4 (BMP-4), mutant bone morphogenic protein-5 (BMP-5) (precursor only), mutant bone morphogenic protein-6 (BMP-6)/Vgfr1, mutant bone morphogenic protein-7 (BMP-7)/osteogenic protein (OP)-1, mutant bone

morphogenic protein-8 (BMP-8)/osteogenic protein (OP)-2, mutant bone morphogenic protein-10 (BMP-10), mutant bone morphogenic protein-11 (BMP-11), mutant bone morphogenic protein-15 (BMP-15), mutant Norrie Disease protein (NDP), mutant Growth/Differentiation Factor-1 (GDF-1), mutant Growth/Differentiation Factor-5 (GDF-5) (precursor only), mutant Growth/Differentiation Factor-8 (GDF-8), mutant Growth/Differentiation Factor-9 (GDF-9), mutant Glial Cell-Derived Neurotrophic Factor (GDNF)/Artemin, and mutant Glial Cell-Derived Neurotrophic Factor (GDNF)/Persephin proteins. Accordingly, the present invention provides methods for using mutant CKGFs, CKGF analogs, fragments, and derivatives thereof for treating or preventing diseases. Pharmaceutical and diagnostic compositions, methods of using mutant CKGF proteins, including TSH heterodimers and TSH analogs with utility for treatment and prevention of metabolic and reproductive diseases are also provided.

Please replace the copy of previously-submitted sequence listing with the Substitute Sequence Listing submitted herewith.